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EDITORIAL COMMENT

Is There More to the Calcium Scan Than Just Coronary Calcium?*

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More than 25 years ago, Agatston et al. (1) introduced coronary artery calcification (CAC) quantification by computed tomography (CT) that was to revolutionize our ability to improve risk assessment in cardiovascular disease (CVD). The South Bay Heartwatch (2,3) and other investigations (4-6) initially showed CAC assessed by fluoroscopy (2) and CT (3-6) predicted coronary heart disease (CHD) events, even beyond the Framingham Risk Score (FRS) (3). Subsequently, the MESA (Multi-ethnic Study of Atherosclerosis) study showed the incremental value of CAC over risk factors (7) and, importantly, added net risk reclassification (8). Yeboah et al. (9) further showed the added usefulness of CAC beyond risk factors to be far more than what other screening modalities, biomarkers, or family history provided. These and other investigations supported the use of CAC screening guidelines for CHD risk assessment, recently noting CAC to be the "most useful of the current approaches to improving risk assessment among individuals found to be at intermediate risk after formal risk assessment" (10).

Beyond CAC as a sound measure of subclinical atherosclerosis, we and others have examined thoracic aortic calcification (TAC) (11,12), aortic valve calcification (AVC) (13,14), and, most recently, abdominal aortic calcification (15,16) for predicting CVD events and mortality. In MESA, Budoff et al. (12) showed TAC predicted future CVD events over risk factors and CAC, but in women only, whereas another cohort study showed no added risk prediction (11). Further, AVC independently predicted CVD mortality, but not overall coronary or cardiac events over CAC (13) and in another cohort AVC predicted of total mortality beyond CAC (14). Although Criqui et al. (15) in MESA also showed abdominal aortic calcification to predict CVD and total mortality better than CAC, there is added radiation, acquisition, and interpretation time beyond CAC alone. Extracoronary calcification (aortic valve, aortic root, mitral valve, or thoracic aorta) also improved prediction of mortality, but with only a slight improvement in C-statistic beyond risk factors and CAC (0.799 to 0.802) (16). Allison et al. (17) showed multisite calcification from the carotid, thoracic aorta, or iliac arteries to predict total mortality, but without improvement in C-statistic beyond risk factors and CAC. The question remains whether and to what extent we are able to improve on risk assessment beyond that afforded by standard risk assessment and a noncontrast CT scan evaluating CAC. And more important, can information from these measures affect clinical decision making beyond that provided by CAC alone?

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In this issue of *iJACC*, Mahabadi et al. (18) have examined whether a combination of noncoronary measures from the noncontrast CT scan further improves risk stratification from the well-characterized Heinz Nixdorf Recall study of 3,630 subjects followed for 10 years. Only left atrial index, epicardial adipose tissue volume, and TAC together (but not individually) slightly improved risk prediction beyond FRS and CAC (C-statistic 0.756 vs. 0.749; $p = 0.01$), although with a net reclassification index (NRI) of 38%. In contrast, the improvement in C-statistic was much greater from adding CAC on top of FRS alone (0.749 vs. 0.700). Improvement in C-statistic from adding these noncoronary measures was best in those at intermediate risk (FRS of 10% to 20%), but the NRI was least in this group (14.5%; not significant), the only group where CAC screening is appropriate in, thus limiting the clinical value of these measures. Although TAC, left atrial, and left ventricular measures can be done relatively quickly in conjunction with CAC measures, it is not clear if

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the added time to do epicardial adipose tissue measures and minimal improvement in C-statistic and NRI can justify doing these measures routinely. In fact, in MESA, Yeboah et al. (19), who measured TAC, AVC, mitral annular calcification, pericardial adipose tissue volume, and liver attenuation, did not find any of these measures to improve risk or reclassification, and unexpectedly these measures reduced the C-statistic in those at intermediate risk. Also, the NRI Mahabadi et al. (18) observed was greatest (59.7%) in those without CAC, suggesting clinical usefulness in those we already know have at least a 15-year "warranty" against total mortality (20).

Mahabadi et al. (18) have conducted an ambitious and carefully done study in the renowned Heinz-Nixdorf cohort, but the relatively modest added risk prediction and limited clinical usefulness of their trio of epicardial adipose tissue, TAC, and left atrial size measures, along with the "modest at best" added value of noncoronary CT measures studied by others, suggests assessing these measures beyond CAC in routine CVD risk assessment is not ready for prime time. Further study is warranted to examine whether in selected patient subgroups selected non-CAC CT measures can be best used to influence further diagnostic or treatment decisions and if longer follow-up from Heinz-Nixdorf, MESA, and other studies may yield greater power to examine relationships between certain noncoronary measures and non-CHD events not observed when looking at composite CHD or CVD endpoints, as most studies have been limited to doing so to date.

Because the strong prognostic significance of CAC has now been established for >15 years from studies involving collectively tens of thousands of subjects, our efforts are best spent focusing on promoting appropriate CAC-guided CVD risk assessment in populations proven to show a benefit and with clear guidelines for their use (10). The utopia of more perfect CVD risk prediction is still in the future, but CAC scanning has provided us with a great start for the present, with the evidence overwhelmingly favorable for CAC having a central role in CVD risk assessment.

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